

PRELIMINARY AMENDMENT  
U.S. Appln. No.: 10/576,496

Atty. Docket No.: Q94468

**AMENDMENTS TO THE CLAIMS**

**This listing of claims will replace all prior versions and listings of claims in the application:**

**LISTING OF CLAIMS:**

1. **(original):** A method for obtaining a disease-associated gene, wherein a disease-associated transcription factor is expressed in a cell line that is deficient in said transcription factor or in a primary cultured cell, and the gene the expression of which is thereby induced or inhibited is screened.

2. **(currently amended):** ~~A method for obtaining~~ The method according to claim 1, ~~wherein the disease-associated gene is a~~ Runx2/Cbfa1-related disease-associated gene, ~~and~~ wherein Runx2/Cbfa1 is expressed in a Runxs/Cbfa1-deficient chondrocyte cell line or in a Runx2/Cbfa1-deficient primary cultured cell, and the gene the expression of which is thereby induced or inhibited is screened.

3. **(currently amended):** ~~A method for obtaining~~ The method according to claim 2, ~~wherein the Runx2/Cbfa1-related disease-associated gene is a~~ gene associated with regulation of cartilage differentiation, ~~and~~ wherein Runx2/Cbfa1 is expressed in a Runx2/Cbfa1-deficient chondrocyte cell line or in a Runx2/Cbfa1-deficient primary cultured cell, and the gene the expression of which is thereby induced or inhibited is screened.

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4. **(original):** The method according to any one of claims 1 to 3, wherein said screening is carried out via subtraction or DNA chip analysis.

5. **(original):** A primary chondrocyte or cultured chondrocyte derived from a Runx2/Cbfa1-deficient mouse.

6. **(original):** A chondrocyte derived from a Runx2/Cbfa1- and p53-deficient mouse.

7. **(original):** The chondrocyte cell line derived from the Runx2/Cbfa1- and p53-deficient mouse according to claim 6, which is the RU-1 cell line or the RU-22 cell line deposited under the accession number FERM BP-10137 or FERM BP-10138 at the International Patent Organism Depositary of the National Institute of Advanced Industrial Science and Technology.

8. **(canceled).**

9. **(original):** A polynucleotide having the nucleotide sequence shown in SEQ ID NO: 9.

10. - 14. **(canceled).**

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15. **(currently amended):** A human homolog polynucleotide of the polynucleotide according to claim 89, which has the nucleotide sequence shown in SEQ ID NO: ~~27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, or 51.~~

16. **(currently amended):** A polynucleotide having 65% or more homology to the polypeptide encoded by the polynucleotide having the nucleotide sequence shown in SEQ ID NO: ~~1, 3, 5, 7, 9 or, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, or 51,~~ and encoding a protein capable of stimulating or inhibiting cartilage differentiation.

17. **(currently amended):** A polynucleotide being capable of hybridizing under stringent conditions to the polynucleotide having the nucleotide sequence shown in SEQ ID NO: ~~1, 3, 5, 7, 9 or, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, or 51~~ or a complementary strand thereof, and encoding a protein capable of stimulating or inhibiting cartilage differentiation.

18. **(currently amended):** A recombinant DNA vector comprising the polynucleotide according to any one of claims 9, 15, 16, and 17 ~~8 to 17~~ or a complementary strand thereof.

19. **(original):** A transformant transformed with the recombinant DNA vector according to claim 18.

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20. (currently amended): A polypeptide comprising the amino acid sequence shown in SEQ ID NO: ~~2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, or 52.~~

21. (currently amended): A polypeptide comprising an amino acid sequence derived from the amino acid sequence shown in SEQ ID NO: ~~2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, or 52~~ by deletion, substitution, or addition of one or several amino acid residues, and capable of stimulating or inhibiting cartilage differentiation.

22. (currently amended): A polypeptide comprising an amino acid sequence having at least 65% homology to the amino acid sequence shown in SEQ ID NO: ~~2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, or 52,~~ and capable of stimulating or inhibiting cartilage differentiation.

23. - 30. (canceled).

31. (currently amended): A pharmaceutical composition comprising the polynucleotide having the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51, a polynucleotide having 65% or more homology to the polypeptide encoded by the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51 and

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encoding a protein capable of stimulating or inhibiting cartilage differentiation, or a polynucleotide being capable of hybridizing under stringent conditions to the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51 and encoding a protein capable of stimulating or inhibiting cartilage differentiation, according to any one of claims 8 to 17 and a pharmaceutically acceptable carrier.

**32. (currently amended):** A method for preventing and/or treating a bone and/or joint disease comprising administering to a subject the polynucleotide ~~according to any one of claims 8 to 17~~ having the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51, a polynucleotide having 65% or more homology to the polypeptide encoded by the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51 and encoding a protein capable of stimulating or inhibiting cartilage differentiation, or a polynucleotide being capable of hybridizing under stringent conditions to the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51 and encoding a protein capable of stimulating or inhibiting cartilage differentiation.

**33. (previously presented):** The method according to claim 32, wherein the bone and/or joint disease is osteoarthritis.

**34. (currently amended):** A method for diagnosing a disease comprising contacting a sample with the polynucleotide ~~according to any one of claims 8 to 17~~ having the nucleotide

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sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51, a polynucleotide having 65% or more homology to the polypeptide encoded by the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51 and encoding a protein capable of stimulating or inhibiting cartilage differentiation, or a polynucleotide being capable of hybridizing under stringent conditions to the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51 and encoding a protein capable of stimulating or inhibiting cartilage differentiation.

**35. (currently amended):** A method for diagnosing a bone and/or joint disease comprising contacting a sample with the polynucleotide ~~according to any one of claims 8 to 17~~ having the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51, a polynucleotide having 65% or more homology to the polypeptide encoded by the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51 and encoding a protein capable of stimulating or inhibiting cartilage differentiation, or a polynucleotide being capable of hybridizing under stringent conditions to the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51 and encoding a protein capable of stimulating or inhibiting cartilage differentiation.

**36. (previously presented):** The method according to claim 35, wherein the bone and/or joint disease is osteoarthritis.

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37. (currently amended): A transgenic animal model of a bone and/or joint disease, in which an expression level of the gene encoded by the polynucleotide ~~according to any one of claims 8 to 17~~ having the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51, a polynucleotide having 65% or more homology to the polypeptide encoded by the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51 and encoding a protein capable of stimulating or inhibiting cartilage differentiation, or a polynucleotide being capable of hybridizing under stringent conditions to the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51 and encoding a protein capable of stimulating or inhibiting cartilage differentiation is enhanced or lowered.

38. (currently amended): A transgenic mouse model of a bone and/or joint disease, in which the gene encoded by the polynucleotide ~~according to any one of claims 8 to 17~~ having the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51, a polynucleotide having 65% or more homology to the polypeptide encoded by the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51 and encoding a protein capable of stimulating or inhibiting cartilage differentiation, or a polynucleotide being capable of hybridizing under stringent conditions to the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51 and encoding a protein capable of stimulating or inhibiting cartilage differentiation is expressed with the use of a type II collagen promoter.

39. - 94. (canceled).